REMARKS

Claims 145, 147, and 149-154 are pending in the application. Claims 145 and 154 have been amended. Support for the amendments can be found throughout the instant specification and specifically on page 8, lines 26-29, page 9, lines 25-28, page 10, lines 15-16, page 11, lines 5-7 and page 47, lines 7-9. No new matter has been introduced.

Amendment or cancellation of claims should in no way be construed as an acquiescence, narrowing, or surrender of any subject matter. Amendments or cancellations have been made not only to point out with particularity and to claim the present invention, but also to expedite prosecution of the present application. Applicants reserve the option to prosecute the originally filed claims further, or similar ones, in the instant or subsequently filed patent applications.

Priority

The Examiner has maintained the objection to the instant claims for reciting "limitations which were not clearly disclosed in the priority applications as well as the specification as filed…and do change the scope of the instant disclosure as-filed" (page 4, last paragraph of the instant Office Action). Specifically, the Examiner states, "neither the priority applications nor the instant application have (*sic*) provides a sufficient description of a representative number of species of 'inhibitors of CD40 or CD40 ligand' to represent the entire genus of 'inhibitors of CD40 or CD40 ligand', broadly encompassed by the current claims" (page 5, 1st paragraph of the instant Office Action).

Applicants respectfully traverse the objection. In Applicants' response to the Non-Final Office Action, dated October 9, 2007, claims 145 and 154 were amended deleting the phrase, "inhibitor or the CD40/CD40 ligand costimulatory interaction." Applicants believe the Examiner's objection is considered moot and therefore respectfully request reconsideration and withdrawal of the objection.

Rejection of Claims 145, 147, and 149-154 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 145, 147, and 149-154 under 35 U.S.C. § 112, first paragraph, as allegedly not conveying to one of ordinary skill in the art that Applicants were in

possession of the claimed invention. Specifically, the Examiner states the recitation of "wherein an 'a soluble CD40 ligand or CD40 receptor' is not administered to the transplant recipient" is not readily apparent either in the pending or in the earlier priority documents."

As the Examiner is aware, "[a]ny negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977)" (MPEP 2173.05(i) Negative Limitations).

Applicants respectfully traverse the rejection. However, solely in order to expedite prosecution and in no way conceding to the Examiner's rejections, Applicants have amended claims 145 and 154, thereby rendering the Examiner's rejection moot. Support for the amendments can be found specifically in priority document U.S.S.N. 09/339,596 (U.S. Pat. 6,913,747) on column 23, lines 6-12 and column 24, lines 54-63. For instance, "[m]ethods of treatment also involve co-administration of a humanized anti-B7-2 antibody or humanized anti-B7-1 antibody with other standard therapy drugs (e.g., a drug that is used to modulate the immune response of an individual having a transplanted organ, tissue, cell or the like), such as methotrexate, rapamycin, cyclosporin, steroids, anti-CD40 antibodies, and analogs thereof" (col. 23, lines 6-12). Support can also be found in the instant specification on page 8, lines 26-29, page 9, lines 25-28, page 10, lines 15-16, page 11, lines 5-7 and page 47, lines 4-9. For instance, the instant specification recites, "the humanized B7-1 and/or B7-2 antibodies and/or other composition are administered at times to treat the diseases described herein or induce tolerization (e.g., methotrexate; rapamycin; cyclosporin; steroids; anti-CD40 pathway inhibitors such as anti-CD40 antibodies, anti-CD40 ligand antibodies and small molecule inhibitors of the CD40 pathway…)" (page 47, lines 4-8, emphasis added). In short, Applicants use of the term "and/or" adequately supports administration of or, alternatively, no administration of these agents. Indeed, as the Court held in *In re Johnson*, ***"[i]f alternative elements are positively recited in the specification, they may be explicitly excluded in the claims"*** (Emphasis added; see *supra*).

Applicants also respectfully point out that the instant specification contains numerous examples of the administration of B7-1 and B7-2 antibodies in the absence of an anti-CD40 antibody or an anti-CD40 ligand antibody. In particular, Applicants direct the Examiner to Examples 16-23, and Figures 16-23 and 26-28 of the instant specification, all of which

demonstrate the use of B7-1 and B7-2 antibodies without an anti-CD40 antibody or an anti-CD40 ligand antibody. For example, Applicants point out that Example 22 of the instant specification discloses the use of B7-1 and B7-2 antibodies alone and in combination with several other immunosuppressive agents, such as cyclosporin A, rapamycin, and steroids, but not an anti-CD40 antibody or an anti-CD40 ligand antibody. Applicant respectfully remind the Examiner that a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a *prima facie* case for lack of descriptive support. *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993), MPEP 213.05(i). Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

Rejection of Claims 145, 147, and 154 Under 35 U.S.C. § 102(e)

The Examiner has rejected claims 145, 147, and 154 under 35 U.S.C. § 102(e), as allegedly being anticipated by Freeman *et al.* (U.S. Patent No. 6,605,279). The Examiner states that "it is reasonable to conclude that the same patient is being administered the same active agent by the same mode of administration in the same amount in both the instant claims and the prior art reference" (page 10, paragraph 5 of the instant Office Action). Specifically, the Examiner reiterates that "Freeman *et al.* teaches methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents such as cyclosporine or FK506, including it [sic] usefulness in situations of tissue and organ transplantation as well as in GVHD (see entire document, particularly Other Therapeutic Reagents on columns 32-34)" (page 11, 1st paragraph of the instant Office Action).

Applicants respectfully traverse the rejection. Applicants submit herewith a Declaration under 37 C.F.R. §1.132 by co-inventor Dr. Gary S. Gray. The Declaration states that Dr. Gray conceived of the subject matter disclosed (and not claimed) in U.S. Patent No. 6,605,279, which is relied upon in the pending rejection, thereby removing the '279 patent as a valid §102(e) reference. Applicants believe this renders the Examiner's rejection moot. Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

Rejection of Claims 145, 147, and 149-154 Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 145, 147, and 149-154 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Freeman *et al.* (U.S. Patent No. 6,605,279) in view of de Boer *et al.* (U.S. Patent No. 5,747,034[1]). Specifically, the Examiner contends that the deficiencies noted for Freeman *et al.* is remedied by de Boer *et al.*, which "teach[es] the use of B7-specific antibodies in combination with immunosuppressive agents such as cyclosporin, FK506 and rapamycin (e.g., see column 14, paragraphs 2-3) in therapeutic amounts and modes of administration encompassed by the claimed invention (e.g., see column 16, paragraph 5) (see entire document)" (page 12 of the instant Office Action).

Applicants respectfully traverse the rejection. As described *supra*, Applicants submit herewith a Declaration under 37 C.F.R. §1.132 by co-inventor Dr. Gary S. Gray, removing Patent No. 6,605,279 as a valid §102(e) and 103(a) reference. Applicants believe that this renders the rejection under 35 U.S.C. § 103(a) moot, since the primary reference is no longer valid. Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

[1] The Examiner has listed U.S. Patent No. 5,757,034 as the patent corresponding to de Boer *et al.* Based on the Information Disclosure Statement filed February 3, 2003, Applicants believe that the Examiner intended to refer to U.S. Patent No. 5,747,034.

CONCLUSION

Early and favorable reconsideration of the application is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1000. If any fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to **Deposit Account No. 06-1448, WYS-004.01.**

Respectfully submitted,
FOLEY HOAG

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